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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/500,606 | 05/05/2005 | Maria Cristina Geroni | 17703 (PC27210A) | 4724 |
| 7590 11/12/2008 | | | | |
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| ART UNIT | | PAPER NUMBER | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/500,606

Applicant(s)

GERONI ET AL.

Examiner

WALTER E. WEBB

Art Unit

1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 July 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-11,13-15 and 24-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-11, 13-15 and 24-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/888)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicants' arguments, filed 7/15/2008, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112--Previous

Claims 2 and 10 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant argues that CP-564959, ZD-2171 and CI-202 are well known terms in the medical field, and therefore the meaning and scope of these terms would be readily be understood by a person skilled in the art. However, these are laboratory designations which are subject to the same imprecision as trademarks and tradenames, as previously discussed. Accordingly, claims 2 and 10 remain rejected as being indefinite. Applicant should replace these laboratory designations with chemical names or structures.

Claim Rejections - 35 USC § 103--Previous

Claims 1-3, 5-11, 13-15 and 24-30 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cozzi et al. in view of Sironak et al., and further in view of Grimley et al. This rejection also applies to newly amended claims 31-34.

Applicant argues that the examples of antitumor agents taught by Cozzi to be combined with their acryloyl distamycin compounds are not protein kinase inhibitors as claimed. Applicant also argues that Cozzi et al. does not teach a protein kinase inhibitor having a synergistic antineoplastic effect. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. As previously stated, the motivation to combine the compounds of Cozzi with a protein kinase inhibitor stems from the fact that some protein kinase inhibitors, like the compound of Sironak, are useful in treating cancer. In regard to having a "synergistic antineoplastic effect," as previously stated, a person of ordinary skill in the art would reasonably expect a synergistic effect in light of the fact that Sirotnak et al. teach that the coadministration of a protein kinase inhibitor (ZD1839) **enhance** the efficacy of cytotoxic agents, and demonstrates a more than additive effect when coadministered with a known cytotoxic agent.

Applicant further argues that there would be no basis to make a generalization that if ZD 1839 and another compound are taught to be useful in treating lung cancer individually, then combination of the two would produce a synergistic effect in the treatment of lung cancer. However, it was stated previously that a synergistic effect would be reasonably expected in light of the teachings of Sirotnak. In other words, the artisan should not be surprised to see a synergistic effect, since ZD 1839 is known to enhance the efficacy of cytotoxic agents. Other effects continue to exist, however obviousness requires only a reasonable expectation of success. Based on the teachings of Sirotnak the artisan would reasonably expect a synergistic effect.

In further support of their argument applicant cites, G. Giaccone et al., showing that ZD 1839 combined with gemcitabine and cisplatin in chemotherapy-naïve patients had no improved efficacy over gemcitabine and cisplatin alone. However, the issue is not whether the artisan would combine ZD1839 with any cytotoxic agent, but whether the artisan would combine ZD1839 with the compound(s) of Cozzi. As previously argued the motivation to combine the compound(s) of Cozzi with ZD1839 stems from the fact that both compound are taught to be useful in treating cancer e.g. lung cancer. The motivation to combine is further enhanced by the fact that the art recognizes ZD1839's usefulness in improving cytotoxicity of a diverse group cytotoxic agents, including a successful treatment of lung cancer. Applicant's argument is unpersuasive since it fails to address the level of expectation the artisan would have in regard to combining a compound of Cozzi with ZD1839.

Applicant argues that "a generalization cannot be made that merely because two different compounds are useful to treat cancer individually, then a person skilled in the art would have reasonable expectation that one compound can substitute another, and be combined with a protein kinase inhibitor to produce synergistic effect in the treatment of lung cancer." This argument is in response to the use of Grimely as a tertiary reference. However, no assertion was made to substitute the indole carbozoles in Grimely with the acryloly distamycin compounds of Cozzi. Grimely was used merely to provide further motivation for combining protein kinases with other cytotoxic agents. Grimely taught that different mechanisms of action from combinations can maximize the toxic effects on target cells, while minimizing toxic effects on non-target cells.

Obvious-type Double Patenting--Previous

Claims 1-3, 5-11, 13-15 and 24-30 remain rejected on the ground of nonstatutory obvious-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,482,920 (Cozzi) in view of Sirotnak et al. The rejection also applies to newly amended claims 31-34.

Applicant relies on the same arguments above with regard to this obvious-type double patenting rejection.

For the reasons stated above in the 35 USC § 103(a) rejection, the rejection under the obvious-type double patenting is also maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612